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Environmental Protection Agency  
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Washington, D.C. 20460  
Attn: Section 8(e) Coordinator (CAP Agreement)

8EHQ-92-12389  
INIT  
88220010598

Dear Coordinator:

8ECAP-0025

On behalf of the Regulatee and pursuant to Unit II B.1.b. and Unit II C of the 6/28/91 CAP Agreement, E.I. Du Pont de Nemours and Co. hereby submits (*in triplicate*) the attached studies. Submission of this information is voluntary and is occasioned by unilateral changes in EPA's standard as to what EPA now considers as reportable information. Regulatee's submission of information is made solely in response to the new EPA §8(e) reporting standards and is not an admission: (1) of TSCA violation or liability; (2) that Regulatee's activities with the study compounds reasonably support a conclusion of substantial health or environmental risk or (3) that the studies themselves reasonably support a conclusion of substantial health or environmental risk.

The "Reporting Guide" creates new TSCA 8(e) reporting criteria which were not previously announced by EPA in its 1978 Statement of Interpretation and Enforcement Policy, 43 Fed Reg 11110 (March 16, 1978). The "Reporting Guide" states criteria which expands upon and conflicts with the 1978 Statement of Interpretation. Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" raises significant due processes issues and clouds the appropriate reporting standard by which regulated persons can assure TSCA Section 8(e) compliance.

For Regulatee,

Mark H. Christman  
Counsel  
Legal D-7158  
1007 Market Street  
Wilmington, DE 19898  
(302) 774-6443

2/13/95

## ATTACHMENT 1

Submission of information is made under the 6/28/91 CAP Agreement, Unit II. This submission is made voluntarily and is occasioned by recent changes in EPA's TSCA §8(e) reporting standard; such changes made, for the first time in 1991 and 1992 without prior notice and in violation of Regulatee's constitutional due process rights. Regulatee's submission of information under this changed standard is not a waiver of its due process rights; an admission of TSCA violation or liability, or an admission that Regulatee's activities with the study compounds reasonably support a conclusion of substantial risk to health or to the environment. Regulatee has historically relied in good faith upon the 1978 Statement of Interpretation and Enforcement Policy criteria for determining whether study information is reportable under TSCA §8(e), 43 Fed Reg 11110 (March 16, 1978). EPA has not, to date, amended this Statement of Interpretation.

After CAP registration, EPA provided the Regulatee the June 1, 1991 "TSCA Section 8(e) Reporting Guide". This "Guide" has been further amended by EPA, EPA letter, April 10, 1992. EPA has not indicated that the "Reporting Guide" or the April 1992 amendment supersedes the 1978 Statement of Interpretation. The "Reporting Guide" and April 1992 amendment substantively lowers the Statement of Interpretation's TSCA §8(e) reporting standard<sup>2</sup>. This is particularly troublesome as the "Reporting Guide" states criteria, applied retroactively, which expands upon and conflicts with the Statement of Interpretation.<sup>3</sup> Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" and the April 1992 amendment clouds the appropriate standard by which regulated persons must assess information for purposes of TSCA §8(e).

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<sup>2</sup>In sharp contrast to the Agency's 1977 and 1978 actions to soliciting public comment on the proposed and final §8(e) Policy, EPA has unilaterally pronounced §8(e) substantive reporting criteria in the 1991 Section 8(e) Guide without public notice and comment. See 42 Fed Reg 45362 (9/9/77), "Notification of Substantial Risk under Section 8(e): Proposed Guidance".

<sup>3</sup>A comparison of the 1978 Statement of Interpretation and the 1992 "Reporting Guide" is appended.

Throughout the CAP, EPA has mischaracterized the 1991 guidance as reflecting "longstanding" EPA policy concerning the standards by which toxicity information should be reviewed for purposes of §8(e) compliance. Regulatee recognizes that experience with the 1978 Statement of Interpretation may cause a review of its criteri. Regulatee supports and has no objection to the Agency's amending reporting criteria *provided that* such amendment is not applied to the regulated community in an unfair way. However, with the unilateral announcement of the CAP under the auspices of an OCM enforcement proceeding, EPA has wrought a terrific unfairness since much of the criteria EPA has espoused in the June 1991 Reporting Guide and in the Agency's April 2, 1992 amendment is new criteria which does not exist in the 1978 Statement of Interpretation and Enforcement Policy.

The following examples of new criteria contained in the "Reporting Guide" that is not contained in the Statement of Interpretation follow:

- o even though EPA expressly disclaims each "status report" as being preliminary evaluations that should not be regarded as final EPA policy or intent<sup>4</sup>, the "Reporting Guide" gives the "status reports" great weight as "sound and adequate basis" from which to determine mandatory reporting obligations. ("Guide" at page 20).
- o the "Reporting Guide" contains a matrix that establishes new numerical reporting "cutoff" concentrations for acute lethality information ("Guide" at p. 31). Neither this matrix nor the cutoff values therein are contained in the Statement of Interpretation. The regulated community was not made aware of these cutoff values prior to issuance of the "Reporting Guide" in June, 1991.
- o the "Reporting Guide" states new specific definitional criteria with which the Agency, for the first time, defines as 'distinguishable neurotoxicological effects'; such criteria/guidance not expressed in the 1978 Statement of Interpretation.<sup>5</sup>
- o the "Reporting Guide" provides new review/ reporting criteria for irritation and sensitization studies; such criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy.
- o the "Reporting Guide" publicizes certain EPA Q/A criteria issued to the Monsanto Co. in 1989 which are not in the Statement of Interpretation; have never been published in the Federal Register or distributed by the EPA to the Regulatee. Such Q/A establishes new reporting criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy.

<sup>4</sup>The 'status reports' address the significance, if any, of particular information reported to the Agency, rather than stating EPA's interpretation of §8(e) reporting criteria. In the infrequent instances in which the status reports contain discussion of reportability, the analysis is invariably quite limited, without substantial supporting scientific or legal rationale.

<sup>5</sup> See, e.g., 10/2/91 letter from Du Pont to EPA regarding the definition of 'serious and prolonged effects' as this term may relate to transient anesthetic effects observed at lethal levels; 10/1/91 letter from the American Petroleum Institute to EPA regarding clarification of the Reporting Guide criteria.

In discharging its responsibilities, an administrative agency must give the regulated community fair and adequate warning to as what constitutes noncompliance for which penalties may be assessed.

Among the myriad applications of the due process clause is the fundamental principle that statutes and regulations which purport to govern conduct must give an adequate warning of what they command or forbid.... Even a regulation which governs purely economic or commercial activities, if its violation can engender penalties, must be so framed as to provide a constitutionally adequate warning to those whose activities are governed.

Diebold, Inc. v. Marshall, 585 F.2d 1327, 1335-36 (D.C. Cir. 1978). See also, Rollins Environmental Services (NJ) Inc. v. U.S. Environmental Protection Agency, 937 F. 2d 649 (D.C. Cir. 1991).

While neither the are rules, This principle has been applied to hold that agency 'clarification', such as the Statement of Interpretation, the "Reporting Guide" nor the April 1992 amendments will not applied retroactively.

...a federal court will not retroactively apply an unforeseeable interpretation of an administrative regulation to the detriment of a regulated party on the theory that the post hoc interpretation asserted by the Agency is generally consistent with the policies underlying the Agency's regulatory program, when the semantic meaning of the regulations, as previously drafted and construed by the appropriate agency, does not support the interpretation which that agency urges upon the court.

Standard Oil Co. v. Federal Energy Administration, 453 F. Supp. 203, 240 (N.D. Ohio 1978), aff'd sub nom. Standard Oil Co. v. Department of Energy, 596 F.2d 1029 (Em. App. 1978):

The 1978 Statement of Interpretation does not provide adequate notice of, and indeed conflicts with, the Agency's current position at §8(e) requires reporting of all 'positive' toxicological findings without regard to an assessment of their relevance to human health. In accordance with the statute, EPA's 1978 Statement of Interpretation requires the regulated community to use scientific judgment to evaluate the significance of toxicological findings and to determining whether they reasonably support a conclusion of a substantial risk. Part V of the Statement of Interpretation urges persons to consider "the fact or probability" of an effect's occurrence. Similarly, the 1978 Statement of Interpretation stresses that an animal study is reportable only when "it contains reliable evidence ascribing the effect to the chemical." 43 Fed Reg. at 11112. Moreover, EPA's Statement of Interpretation defines the substantiality of risk as a function of both the seriousness of the effect and the probability of its occurrence. 43 Fed Reg 11110 (1978). Earlier Agency interpretation also emphasized the "substantial" nature of a §8(e) determination. See 42 Fed Reg 45362, 45363

(1977). [Section 8(e) findings require "extraordinary exposure to a chemical substance...which critically imperil human health or the environment"].

The recently issued "Reporting Guide" and April 1992 Amendment guidance requires reporting beyond and inconsistent with that required by the Statement of Interpretation. Given the statute and the Statement of Interpretation's explicit focus on substantial human or environmental risk, whether a substance poses a "substantial risk" of injury requires the application of scientific judgment to the available data on a case-by-case basis.

If an overall weight-of-evidence analysis indicates that this classification is unwarranted, reporting should be unnecessary under §8(e) because the available data will not "reasonably support the conclusion" that the chemical presents a substantial risk of serious adverse consequences to human health.

Neither the legislative history of §8(e) nor the plain meaning of the statute support EPA's recent lowering of the reporting threshold that TSCA §8(e) was intended to be a sweeping information gathering mechanism. In introducing the new version of the toxic substances legislation, Representative Eckhart included for the record discussion of the specific changes from the version of H. R. 10318 reported by the Consumer Protection and Finance Subcommittee in December 1975. One of these changes was to modify the standard for reporting under §8(e). The standard in the House version was changed from "causes or contributes to an unreasonable risk" to "causes or significantly contributes to a substantial risk". This particular change was one of several made in TSCA §8 to avoid placing an undue burden on the regulated community. The final changes to focus the scope of Section 8(e) were made in the version reported by the Conference Committee.

The word "substantial" means "considerable in importance, value, degree, amount or extent". Therefore, as generally understood, a "substantial risk" is one which will affect a considerable number of people or portion of the environment, will cause serious injury and is based on reasonably sound scientific analysis or data. Support for the interpretation can be found in a similar provision in the Consumer Product Safety Act. Section 15 of the CPSA defines a "substantial product hazard" to be:

"a product defect which because of the pattern of defect, the number of defective products distributed in commerce, the severity of the risk, or otherwise, creates a substantial risk of injury to the public."

Similarly, EPA has interpreted the word 'substantial' as a quantitative measurement. Thus, a 'substantial risk' is a risk that can be quantified, See, 56 Fed Reg 32292, 32297 (7/15/91). Finally, since information pertinent to the exposure of humans or the environment to chemical substances or mixtures may be obtained by EPA through Sections 8(a) and 8(d) regardless of the degree of potential risk, §8(e) has specialized function. Consequently, information subject to §8(e) reporting should be of a type which would lead a reasonable man to conclude that some type action was required immediately to prevent injury to health or the environment.

## Attachment

**Comparison:**

Reporting triggers found in the 1978 "Statement of Interpretation/ Enforcement Policy", 43 Fed Reg 11110 (3/16/78) and the June 1991 *Section 8(e) Guide*.

<b>TEST TYPE</b> _____	<b>1978 POLICY CRITERIA EXIST?</b>	<b>New 1991 GUIDE CRITERIA EXIST?</b>
<b>ACUTE LETHALITY</b>		
Oral	N}	Y}
Dermal	N}	Y}
Inhalation (Vapors)	N} <sup>6</sup>	Y} <sup>7</sup>
aerosol	N}	Y}
dusts/ particles	N}	Y}
<b>SKIN IRRITATION</b>	N	Y <sup>8</sup>
<b>SKIN SENSITIZATION (ANIMALS)</b>	N	Y <sup>9</sup>
<b>EYE IRRITATION</b>	N	Y <sup>10</sup>
<b>SUBCHRONIC (ORAL/DERMAL/INHALATION)</b>	N	Y <sup>11</sup>
<b>REPRODUCTION STUDY</b>	N	Y <sup>12</sup>
<b>DEVELOPMENTAL TOX</b>	Y <sup>13</sup>	Y <sup>14</sup>

<sup>6</sup>43 Fed Reg at 11114, comment 14:

"This policy statements directs the reporting of specific effects when unknown to the Administrator. Many routine tests are based on a knowledge of toxicity associated with a chemical. unknown effects occurring during such a range test may have to be reported if they are those of concern to the Agency and if the information meets the criteria set forth in Parts V and VII."

<sup>7</sup>Guide at pp.22, 29-31.

<sup>8</sup>Guide at pp-34-36.

<sup>9</sup>Guide at pp-34-36.

<sup>10</sup>Guide at pp-34-36.

<sup>11</sup>Guide at pp-22; 36-37.

<sup>12</sup>Guide at pp-22

<sup>13</sup>43 Fed Reg at 11112

"Birth Defects" listed.

<sup>14</sup>Guide at pp-22

NEUROTOXICITY	N	Y <sup>15</sup>
CARCINOGENICITY	Y <sup>16</sup>	Y <sup>17</sup>
MUTAGENICITY		
<i>In Vitro</i>	Y <sup>18</sup>	Y <sup>19</sup>
<i>In Vivo</i>	Y}	Y}
ENVIRONMENTAL		
Bioaccumulation	Y}	N
Bioconcentration	Y} <sup>20</sup>	N
Oct/water Part. Coeff.	Y}	N
Acute Fish	N	N
Acute Daphnia	N	N
Subchronic Fish	N	N
Subchronic Daphnia	N	N
Chronic Fish	N	N
AVIAN		
Acute	N	N
Reproductive	N	N
Reproductive	N	N

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<sup>15</sup>Guide at pp-23; 33-34.

<sup>16</sup>43 Fed Reg at 11112  
"Cancer" listed

<sup>17</sup>Guide at pp-21.

<sup>18</sup>43 Fed Reg at 11112; 11115 at Comment 15

"Mutagenicity" listed/ *in vivo* vs *in vitro* discussed; discussion of "Ames test".

<sup>19</sup>Guide at pp-23.

<sup>20</sup>43 Fed Reg at 11112; 11115 at Comment 16.



CAS # 1680-21-3; 109-16-0; 868-77-9; 2358-84-1

Chem: Triethylene glycol diacrylate; triethylene glycol dimethacrylate; 2-hydroxyethyl methacrylate; diethylene glycol dimethacrylate

Title: Skin irritation and sensitization tests on guinea pigs

Date: 3/6/69

Summary of Effects: Strong primary irritant

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Copies to: C. W. Maynard, Jr. (6)  
H. G. Gerlach, Jr. (3)

E. I. du Pont de Nemours and Company  
Haskell Laboratory for Toxicology and Industrial Medicine

HASKELL LABORATORY REPORT NO. 48-69

MR NO. 116

Materials Tested:

- Triethylene Glycol Diacrylate (> 98%) a)
- Triethylene Glycol Dimethacrylate (98Z)
- 2-Hydroxyethyl Methacrylate (> 98Z)
- Diethylene Glycol Dimethacrylate (> 98Z)

Haskell Nos.

- 5812
- 5813
- 5814
- 5815

Other Codes

- TDA; ORNB 95-74-1
- TDMA; ORNB 95-74-2
- HEMA; ORNB 95-74-3
- DDMA; ORNB 95-74-4

Materials Submitted by: C. W. Maynard, Jr., Organic Chemicals Department  
Jackson Laboratory

SKIN IRRITATION AND SENSITIZATION TESTS ON GUINEA PIGS

Procedure: Each compound was tested on a group of 15 male albino guinea pigs. To evaluate primary irritation, 0.05 ml of the test material in varying concentrations in 1:1 acetone dioxane containing 1% guinea pig fat (f.a.d.) was applied to the intact shaved skin of the 15 animals. Sensitizing treatments were given during a three-week interval and consisted of: (1) nine topical applications of 0.05 ml test material in f.a.d.; (2) to abraded skin of the first five animals; and (3) four 0.1 ml intradermal injections (i.d.) of 1% test material in dimethylphthalate (DMP) to the second five animals; and (3) two 0.1 ml (i.d.) injections of Freund's Complete Adjuvant followed one and one-half hours later by a 0.1 ml of 1% test material in DMP to the remaining five animals. Following a two-week rest period, the 15 animals in each group were challenged (I) with applications to intact and abraded skin of 0.05 ml test material in f.a.d. Since this challenge produced unexpected negative results, one week later (two weeks later for TDMA) flank patches (0.05 ml) of the highest practical concentrations of test materials were applied. After another rest period, the animals were again challenged (II) with 0.05 ml applications to intact and abraded skin.

- a) Impurities 1) 60 ppm Hydroquinone
- 2) 60 ppm Hydroquinone
- 3) 100 ppm 4-Methoxy hydroquinone
- 4) 60-100 ppm Hydroquinone

- b) Concentrations of nine topical applications 1) TDA - 0.25% x 9
- 2) TDMA - 5.0% x 1 and 10% x 8
- 3) HEMA - 25% x 9
- 4) DDMA - 25% x 9

- c) Concentrations of flank patches 1) TDA - 5% in f.a.d.
- 2) TDMA - 25% in f.a.d. and undiluted
- 3) HEMA - undiluted
- 4) DDMA - undiluted

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## Results:

Chemical	Group	Av. Wt. (g)	Z	Primary Irritation Reactions* at 24 hours		Challenge Test I Reactions at 24 hours		Challenge Test II Reactions at 24 hours		No. of Guinea Pigs Sensitized
				Intact	Abraded	Intact	Abraded	Intact	Abraded	
TDA	Test	505 <sup>a)</sup>	1.0	6+++	9++					
			0.5	8++	7+					
		722 <sup>b)</sup>	0.25	8++	7+	2++, 4+, 9N	1+++	5++, 7+, 2 N	1+++	5/15
TDMA	Control	636	0.25	4+	6 N					
					8+	2 N				
	Test	491	98	4+	11 N	4+, 11 N	12+	3 N	1++, 6+, 8N	0/15
HEMA		787	5	2+	13 N					
			2	1+	14 N					
	Control	613	98	1++	6+, 3 N					
DDMA			10	10 N	8+	2 N				
	Test	521	98	3+	12 N	1+, 14 N	7+	8 N	1++, 2+, 12 N	1/15
		761	10	15 N						
DDMA	Control	654	98	1+++	2+, 7N					
			25	2+	8 N					
	Test	494	98	3+	12 N	1+, 14 N	12+	3 N	1+, 14 N	0/15
DDMA		736	10	15 N						
	Control	675	98	3+	7 N					
			25	1+	9 N					

\* Code: N, +, ++, +++ = Negative, mild, moderate and strong erythema.

a) At time of PI Test

b) At time of Challenge Test II

Summary: Triethylene glycol diacrylate (TDA) is a strong primary irritant producing moderate irritation in concentrations as low as 1% and mild irritation at 0.25%. It caused mild skin sensitization in 5/15 guinea pigs. This is in contrast to earlier work where less pure material but stronger concentrations were used in sensitizing 9/10 guinea pigs (Haskell Laboratory Report No. 16-56).

2-Hydroxyethyl methacrylate (HEMA) was not irritating. One animal appeared to have become mildly sensitized because there were reactions on both intact and abraded skin at the second challenge test. Because these reactions did not flare at 24 hours and had faded by 48 hours, the significance of the response is questionable. Neither triethylene glycol dimethacrylate (TDMA) nor diethylene glycol dimethacrylate (DDMA) was irritating nor was there any evidence of sensitization.

On the basis of the above results and previous experience, we would consider TDA to be both a strong skin irritant and sensitizer. In view of the minimal primary irritation and sensitization potential found for TDMA, HEMA and DDMA in guinea pigs, and the relatively lower sensitization activity of methacrylates in general when compared to that of acrylates, any one of the three methacrylates would appear to have sufficiently low dermatitis potential to be considered for use. When the most technically acceptable compound is agreed upon, however, it would be advisable to have a dermatitis risk evaluation study with the final product carried out on human subjects, since man is somewhat more susceptible than guinea pigs with respect to skin sensitization by acrylate and methacrylate compounds.

DBH:dhg

Date: March 6, 1969

Report No. 48-69

Report by:

Dorothy B. Hood

Chief, Dermal Toxicology Section

Approved by:

Gordon J. Stopps  
Assistant Director



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

Mark H. Christman  
Counsel  
E. I. Du Pont De Nemours and Company  
Legal D-7010-1  
1007 Market Street  
Wilmington, Delaware 19898

OFFICE OF  
PREVENTION, PESTICIDES AND  
TOXIC SUBSTANCES

APR 18 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and refer to the reverse side of this page for "EPA Information Requests".

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

Document Processing Center (7407)  
Attn: TSCA Section 8(e) Coordinator  
Office of Pollution Prevention and Toxics  
U.S. Environmental Protection Agency  
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

*Terry R. O'Bryan*  
Terry R. O'Bryan  
Risk Analysis Branch

Enclosure

12389A



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## Triage of 8(e) Submissions

Date sent to triage: APR 20 1995

NON-CAP

CAP

Submission number: 12389A

TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO

AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX

SBTOX

SEN

w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX

CTOX

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GTOX

STOX/ONCO

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CECATS DATA: Submission # 8EHQ-1092-12389 SEQ. A

TYPE INT. SUPP FLWP

SUBMITTER NAME: E.I. Dupont de Nemours and Company

INFORMATION REQUESTED: FLWP DATE

0501 NO INFO REQUESTED

0502 INFO REQUESTED (TECH)

0503 INFO REQUESTED (VOL ACTIONS)

0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:

0670 REFER TO CHEMICAL SCREENING

0678 CAP NOTICE

VOLUNTARY ACTIONS:

0401 NO ACTION REPORTED

0402 STUDIES PLANNED/IN PROGRESS

0403 NOTIFICATION OF WORKING STATUS

0404 LABEL/MSDS CHANGES

0405 PROCESS/HANDLING CHANGES

0406 APP/USE DISCONTINUED

0407 PRODUCTION DISCONTINUED

0408 CONFIDENTIAL

SUB. DATE: 10/15/92 OTS DATE: 10/27/92 CSRAD DATE: 02/13/95

CHEMICAL NAME:

1680-21-3

109-16-0

868-77-9

2358-84-1

INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C
0201 ONCO (HUMAN)	01 02 04	0216 EPI/CLIN	01 02 04	0241 IMMUNO (ANIMAL)	01 02 04
0202 ONCO (ANIMAL)	01 02 04	0217 HUMAN EXPOS (PROD CONTAM)	01 02 04	0242 IMMUNO (HUMAN)	01 02 04
0203 CELL. TRANS (IN VITRO)	01 02 04	0218 HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243 CHEM/PHYS PROP	01 02 04
0204 MUTA (IN VITRO)	01 02 04	0219 HUMAN EXPOS (MONITORING)	01 02 04	0244 CLASTO (IN VITRO)	01 02 04
0205 MUTA (IN VIVO)	01 02 04	0220 ECO/AQUA TOX	01 02 04	0245 CLASTO (ANIMAL)	01 02 04
0206 REPRO/TERATO (HUMAN)	01 02 04	0221 ENV. OCCURENCE/FATE	01 02 04	0246 CLASTO (HUMAN)	01 02 04
0207 REPRO/TERATO (ANIMAL)	01 02 04	0222 EMER INCI OF ENV CONTAM	01 02 04	0247 DNA DAM/REPAIR	01 02 04
0208 NEURO (HUMAN)	01 02 04	0223 RESPONSE REQUEST DELAY	01 02 04	0248 PROD/USE/PROC	01 02 04
0209 NEURO (ANIMAL)	01 02 04	0224 PROD/COMP/CHEM ID	01 02 04	0251 MSDS	01 02 04
0210 ACUTE TOX. (HUMAN)	01 02 04	0225 REPORTING RATIONALE	01 02 04	0299 OTHER	01 02 04
0211 CHR. TOX. (HUMAN)	01 02 04	0226 CONFIDENTIAL	01 02 04		
0212 ACUTE TOX. (ANIMAL)	01 02 04	0227 ALLERG (HUMAN)	01 02 04		
0213 SUB ACUTE TOX (ANIMAL)	01 02 04	0228 ALLERG (ANIMAL)	01 02 04		
0214 SUB CHRONIC TOX (ANIMAL)	01 02 04	0229 METAB/PHARMACO (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	0240 METAB/PHARMACO (HUMAN)	01 02 04		

USE: \_\_\_\_\_

TOXICOLOGICAL CONCERN:

LOW

MED

HIGH

ONGOING REVIEW

YES (DROP/REFER)

NO (CONTINUE)

REFR

NON-CBI INVENTORY

YES

NO

IN TERMINI

CAS SR

UNCLASSIFIED

8 (E) -12389A

M/M/L/L/L/L/L/L

TDA: DERMAL SENSITIZATION IN MALE GUINEA PIGS IS OF MEDIUM CONCERN BASED ON MILD SENSITIZATION (5/15) FROM NINE TOPICAL EXPOSURES IN 3-WEEKS TO 0.05 ML OF TEST SUBSTANCE AT 25% CONCENTRATION (5 ANIMALS), FOUR 0.1 ML INTRADERMAL I.D. INJECTIONS OF 1% TEST MATERIAL IN DIMETHYL PHTHALATE (DMP) (5 ANIMALS) OVER 3 WEEKS, AND TWO 0.1 ML I.D. INJECTIONS OF FREUND'S ADJUVANT FOLLOWED 1.5 HOURS LATER BY 0.1 ML OF 1% TEST MATERIAL IN DMP. FOLLOWING A 2-WEEK REST PERIOD, ANIMALS WERE CHALLENGED WITH 0.05 ML OF TEST SUBSTANCE APPLIED TO INTACT AND ABRADED SKIN. BECAUSE OF UNEXPECTED NEGATIVE RESULTS, FLANK PATCHES OF 0.05 ML OF 5% TEST COMPOUND WERE APPLIED 1 WEEK AFTER CHALLENGE AND ANIMALS WERE RECHALLENGED (0.05 ML ON INTACT AND ABRADED SKIN) AFTER ANOTHER REST PERIOD.

TDA: ACUTE DERMAL IRRITATION IN MALE GUINEA PIGS IS OF MEDIUM CONCERN BASED ON MODERATE IRRITATION FROM EXPOSURE TO 0.05 ML OF TEST SUBSTANCE AT CONCENTRATIONS OF 1.0%, 0.5%, AND 0.25% IN 1:1 ACETONE/DIOXANE CONTAINING 13% GUINEA PIG FAT APPLIED TO INTACT SKIN.

HEMA: DERMAL SENSITIZATION IN MALE GUINEA PIGS IS OF LOW CONCERN BASED ON MILD SENSITIZATION (1/15) FROM NINE TOPICAL EXPOSURES IN 3-WEEKS TO 0.05 ML OF TEST SUBSTANCE AT 5.0% CONCENTRATION (5 ANIMALS), FOUR 0.1 ML INTRADERMAL I.D. INJECTIONS OF 1% TEST MATERIAL IN DIMETHYL PHTHALATE (DMP) (5 ANIMALS) OVER 3 WEEKS, AND TWO 0.1 ML I.D. INJECTIONS OF FREUND'S ADJUVANT FOLLOWED 1.5 HOURS LATER BY 0.1 ML OF 1% TEST MATERIAL IN DMP. FOLLOWING A 2-WEEK REST PERIOD, ANIMALS WERE CHALLENGED WITH 0.05 ML OF TEST SUBSTANCE APPLIED TO INTACT AND ABRADED SKIN. BECAUSE OF UNEXPECTED NEGATIVE RESULTS, FLANK PATCHES OF 0.05 ML OF 5% TEST COMPOUND WERE APPLIED 1 WEEK AFTER CHALLENGE AND ANIMALS WERE RECHALLENGED (0.05 ML ON INTACT AND ABRADED SKIN) AFTER ANOTHER REST PERIOD.

HEMA: ACUTE DERMAL IRRITATION IN MALE GUINEA PIGS IS OF LOW CONCERN BASED ON NO IRRITATION FROM EXPOSURE TO 0.05 ML OF TEST SUBSTANCE AT CONCENTRATIONS OF 98%, 25%, AND 10% IN 1:1 ACETONE/DIOXANE CONTAINING 13% GUINEA PIG FAT APPLIED TO INTACT SKIN.

TDMA: DERMAL SENSITIZATION IN MALE GUINEA PIGS IS OF LOW CONCERN BASED ON NO EVIDENCE OF SENSITIZATION (0/15) FROM NINE TOPICAL EXPOSURES IN 3-WEEKS TO 0.05 ML OF TEST SUBSTANCE AT 25% CONCENTRATION (5 ANIMALS), FOUR 0.1 ML INTRADERMAL I.D. INJECTIONS



OF 1% TEST MATERIAL IN DIMETHYL PHTHALATE (DMP) (5 ANIMALS) OVER 3 WEEKS, AND TWO 0.1 ML I.D. INJECTIONS OF FREUND'S ADJUVANT FOLLOWED 1.5 HOURS LATER BY 0.1 ML OF 1% TEST MATERIAL IN DMP. FOLLOWING A 2-WEEK REST PERIOD, ANIMALS WERE CHALLENGED WITH 0.05 ML OF TEST SUBSTANCE. FOLLOWING A 2-WEEK REST PERIOD, ANIMALS WERE CHALLENGED WITH 0.05 ML OF TEST SUBSTANCE APPLIED TO INTACT AND ABRADED SKIN. BECAUSE OF UNEXPECTED NEGATIVE RESULTS, FLANK PATCHES OF 0.05 ML OF 5% TEST COMPOUND WERE APPLIED 1 WEEK AFTER CHALLENGE AND ANIMALS WERE RECHALLENGED (0.05 ML ON INTACT AND ABRADED SKIN) AFTER ANOTHER REST PERIOD.

TDMA: ACUTE DERMAL IRRITATION IN MALE GUINEA PIGS IS OF LOW CONCERN BASED ON NO IRRITATION FROM EXPOSURE TO 0.05 ML OF TEST SUBSTANCE AT CONCENTRATIONS OF 98%, 10%, 5%, AND 2% IN 1:1 ACETONE/DIOXANE CONTAINING 13% GUINEA PIG FAT APPLIED TO INTACT SKIN.

DDMA: DERMAL SENSITIZATION IN MALE GUINEA PIGS IS OF LOW CONCERN BASED ON NO EVIDENCE OF SENSITIZATION (0/15) FROM NINE TOPICAL EXPOSURES IN 3-WEEKS TO 0.05 ML OF TEST SUBSTANCE AT 25% CONCENTRATION (5 ANIMALS), FOUR 0.1 ML INTRADERMAL I.D. INJECTIONS OF 1% TEST MATERIAL IN DIMETHYL PHTHALATE (DMP) (5 ANIMALS) OVER 3 WEEKS, AND TWO 0.1 ML I.D. INJECTIONS OF FREUND'S ADJUVANT FOLLOWED 1.5 HOURS LATER BY 0.1 ML OF 1% TEST MATERIAL IN DMP. FOLLOWING A 2-WEEK REST PERIOD, ANIMALS WERE CHALLENGED WITH 0.05 ML OF TEST SUBSTANCE APPLIED TO INTACT AND ABRADED SKIN. BECAUSE OF UNEXPECTED NEGATIVE RESULTS, FLANK PATCHES OF 0.05 ML OF 5% TEST COMPOUND WERE APPLIED 1 WEEK AFTER CHALLENGE AND ANIMALS WERE RECHALLENGED (0.05 ML ON INTACT AND ABRADED SKIN) AFTER ANOTHER REST PERIOD.

DDMA: ACUTE DERMAL IRRITATION IN MALE GUINEA PIGS IS OF LOW CONCERN BASED ON NO IRRITATION FROM EXPOSURE TO 0.05 ML OF TEST SUBSTANCE AT CONCENTRATIONS OF 98%, 25%, AND 10% IN 1:1 ACETONE/DIOXANE CONTAINING 13% GUINEA PIG FAT APPLIED TO INTACT SKIN.